REMARKS

Claims 2, 4, 5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 42-68, 70, and 73-79 are pending. Claims 46-61 stand withdrawn. All claims stand rejected under 35 U.S.C. § 103(a). Claims 2, 4, 16-19, 65, 66, 69, and 75 stand rejected for obviousness-type double patenting. Applicants address each of these rejections below.

Claim Amendments

Claims 16, 42, and 75 have been amended to correct typographical errors. No new matter has been added.

Rejections Under 35 U.S.C. § 103(a)

The Office has rejected select claims as unpatentable under 35 U.S.C. § 103(a) as follows:

(1) Claims 2, 4, 16-19, 65, and 66 stand rejected over Nagai et al. (U.S. Patent No. 7,101,685; "Nagai") in view of Yu et al. (Genes Cells 2:457-466, 1997; "Yu") and Hirsch et al. (J. Virol. 70:3741-3752, 1996; "Hirsch"), and as evidenced by Hanke et al. (Vaccine 17:589-596, 1999; "Hanke");

(2) Claims 2, 4, 5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 42-45, 62-66, 68, 70, 73, 75, and 76 stand rejected over Flanagan et al. (J. Gen. Virol. 78:991-997, 1997; "Flanagan") and Seth et al. (Proc. Natl. Acad. Sci. U.S.A. 95:10112-10116, 1998; "Seth") in view of

Yu and Hurwitz et al. (Vaccine 15:533-540, 1997; "Hurwitz"), and as evidenced by Ourmanov et al. (J. Virol. 74:2740-2751, 2000; "Ourmanov"), Hanke, and Nakanishi et al. (J. Control Release 54:61-68, 1998; "Nakanishi");

(3) Claims 78 and 79 stand rejected over Flanagan and Seth in view of Yu and Hurwitz, and further in view of Göttlinger et al. (Proc. Natl. Acad. Sci. U.S.A. 86:5781-5785, 1989; "Göttlinger");

(4) Claims 11-13, 15, and 74 stand rejected over Flanagan in view of Yu and Kast et al. (J. Immunol. 140:3186-3193, 1988; "Kast");

(5) Claim 14 stands rejected over Flanagan in view of Yu and Kast, and further in view of Boutillon et al. (U.S. Patent No. 6,015,564; "Boutillon");

(6) Claim 67 stands rejected over Flanagan in view of Yu and Kast, and further in view of Hanke; and

(7) Claim 77 stands rejected over Flanagan in view of Yu and Kast, and further in view of Göttlinger.

In response, applicants address the Office's asserted *prima facie* case of obviousness and also provide evidence of secondary considerations that demonstrate non-obviousness of the presently-claimed invention, referring throughout to the concurrently-filed Declaration of Dr. Mamoru Hasegawa under 37 C.F.R. § 1.132 ("the Hasegawa Declaration").

Rebuttal of Prima Facie Case

Regarding rejection (1), the Office asserts (page 4): "[A]ccording to the combined teachings [of the cited art], it is apparent that it is well within the levels of the skilled to make such a construct and be reasonably successful to express the S/HIV protein in mammalian cells." This is not the correct legal standard for obviousness. Even assuming arguendo that one of skill in the art would know how to make a given construct if instructed to do so, this would not render the construct itself obvious. Put another way, knowledge of the routine tools of molecular biology does not render an invention obvious merely because it can be made using those tools.

The Office further states (page 5): "[T]he skilled artisan would have had a reasonable expectation of success to express SHIV proteins in a subject with a recombinant sendai virus vector in place of a vaccinia vector since they express HIV protein in comparable levels." Applicants disagree and direct the Office's attention to ¶ 6 of the Hasegawa declaration, which states:

> The prior use of SeV to express an immunodeficiency viral protein would not have provided a skilled artisan with a reasonable expectation of success in modifying a Vaccinia-based vaccine by substituting SeV for Vaccinia virus. This is so because Vaccinia virus is a DNA virus, whereas SeV is a negative-strand RNA virus. RNA and DNA viruses differ not only in terms of structure, but also in terms of functionality and biosynthesis. For example, when a DNA virus infects host cells, the cells transcribe viral DNA to make mRNA and the host cell translation machinery translates the mRNA into protein. In contrast, when SeV infects host cells, SeV genomic RNA (negative strand RNA) is transcribed into antigenomic RNA by the viral RNA-dependent RNA polymerase, the antigenomic RNA is used to replicate the genomic RNA, and copied genomic RNA is transcribed into mRNA, which is translated into protein. In view of these very different replication systems, one skilled in the

art would have had no reasonable expectation of success for use of a negative-strand RNA virus expressing an immunodeficiency viral protein as a vaccine or a vector that can induce an immune response to the immunodeficiency viral protein, even if DNA viruses were known to be useful as gene-transfer vectors for vaccination, and negative-strand RNA viruses were known to be useful as expression vectors.

Thus, neither Nagai, Yu, Hirsch, or Hanke, alone or in combination, would motivate one of skill in the art to arrive at the claimed invention or to have a reasonable expectation of success in practicing the claimed invention.

Turning to rejections (2) through (7), the Office states (page 6) that Yu "cured the deficiency" of Flanagan and Seth in not teaching a Sendai virus vector, and goes on to state (pages 6-7): "Clearly, Yu et al. teach that sendai virus could be used as a gene transfer vector for expressing a nonanalogous viral protein, such as the immunodeficiency virus protein, in place of the vaccinia virus or interchangeably with other known viral vectors." Applicants disagree. As applicants have previously noted, Yu et al. compares Sendai virus with vaccinia virus in terms of the expression level as an expression vector. The fact that Yu et al. compared the two viruses does not mean that Yu et al. was aware the use of V(-) Sendai virus vector for gene transfer. Nowhere in Yu et al. is there a suggestion that vaccinia virus is used as a gene-transfer vector.

Furthermore, the fact that the expression level from Sendai virus is comparable to the vaccinia virus-based expression would not provide a reasonable expectation of success for using Sendai virus as a gene-transfer vector. As discussed above, vaccinia virus and Sendai virus differ in replication and protein expression systems. When used as

a gene-transfer vector, one skilled in the art would not have readily predicted that Sendai virus encoding an immunodeficiency viral protein can serve as a vaccine or can be used to induce an immune response specific to the immunodeficiency viral protein.

Furthermore, the Office contends (page 7) that Hurwitz establishes the feasibility of intranasal multiple inoculation of a Sendai virus in primates. Indeed, Hurwitz teaches that wild-type Sendai virus could survive in the nasal cavity of primates for several days. However, as applicants have already noted, it would not have been obvious as to whether a recombinant Sendai virus expressing an exogenous gene, for example, as presently claimed, persists in the nasal cavity for several days as found for wild-type virus. From the teachings of Hurwitz, either alone or in combination with Flanagan, Seth, or other cited art, one skilled in the art would not have a reasonable expectation of success for using a recombinant Sendai virus vector to achieve replication and protein expression in primate's nasal cavity similar to wild-type Sendai virus.

Turning to Flanagan, which is commonly cited in rejections (2) through (7), this reference teaches using a recombinant adenovirus expressing SIV Gag protein for vaccination. Adenovirus, as well as the vaccinia virus taught in Hirsch and Seth, is a DNA virus. As discussed above, RNA and DNA viruses differ in replication and protein expression systems. Therefore, even if adenovirus expressing an immunodeficiency viral protein is known to be used as a vaccine that induces an immune response to the immunodeficiency protein and Sendai virus is known to express an immunodeficiency

viral protein as an expression vector, one skilled in the art would not have a reasonable expectation of success for using Sendai virus expressing an immunodeficiency viral protein for induction of an immune response specific to the immunodeficiency viral protein.

In addition, applicants note that the only new reference cited by the Office in the present Office Action is Göttlinger. This reference discloses several protease-processed immunodeficiency viral proteins. Göttlinger discloses the effects on capsid protein processing, virion morphogenesis, and virus replication of a series of mutations that prevent myristoylation, inactivate the viral protease, or alter the sequence of the cleavage sites. However, it does not teach that the processed proteins induce an immune response specific to the proteins. One skilled in the art would not have been motivated to combine Göttlinger with Flanagan, Seth, or any of the other cited references.

Thus, none of the art cited by the Office in rejections (2) through (7), including Flanagan, Seth, Yu, Hurwitz, Ourmanov, Hanke, Nakanishi, Göttlinger, Kast, and Boutillon, whether alone or in combination, would motivate one of skill in the art to arrive at the claimed invention or to have a reasonable expectation of success in practicing the claimed invention. In view of the above arguments, as well as the arguments made previously of record, the rejections of all claims under 35 U.S.C. § 103(a) should be withdrawn.

Evidence of Secondary Considerations

In order to provide evidence of secondary considerations demonstrating the non-obviousness of the presently-claimed invention, applicants again direct the Office's attention to the Hasegawa Declaration submitted herewith, as well as to Exhibits A, B, and C to the Hasegawa Declaration.

Exhibit A is a press release of the International AIDS Vaccine Initiative ("IAVI"), dated July 9, 2007, describing the collaboration between IAVI and DNAVEC, in developing a Sendai-virus ("SeV") vector-based human vaccine for AIDS as presently claimed. (See ¶ 8 of the Hasegawa Declaration.)

Exhibit B is an article published in the Daily Yomiuri Online on July 8, 2007, further describing the collaboration between IAVI and DNAVEC in developing a human vaccine for AIDS as presently claimed. (See ¶ 9 of the Hasegawa Declaration.)

Exhibit C is an English translation of an abstract of a DNAVEC press release, dated May 25, 2007, describing a contract between DNAVEC and Shenzhen SiBiono GeneTech Co., Ltd. ("SiBiono") executed on May 25, 2007 concerning the licensing of the AIDS vaccine technology as presently claimed to SiBiono. The original Japanese-language DNAVEC press release is also included in Exhibit C. (See ¶ 10 of the Hasegawa Declaration.)

Dr. Hasegawa states:

> IAVI, the world's largest institution for AIDS study and prevention, has agreed to provide billions of yen of financial support to DNAVEC for the development of a human vaccine for AIDS. IAVI is a global not-for-profit

organization whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. IAVI is operational in 24 countries and is supported by the Bill & Melinda Gates Foundation, the Alfred P. Sloan Foundation, the Foundation for the National Institutes of Health, and many other organizations and national governments. (See paragraphs 4, 5, and 10 of Exhibit A, and paragraphs 1 and 8 of Exhibit B.)

...Most of the approximately 30 candidate AIDS vaccines in clinical trials are based on a cell-mediated approach, targeting only one arm of the human immune system, and none have been developed for practical use. The SeV vaccine candidate under development by DNAVEC is designed to be administered intranasally in order both to stimulate immune responses in the blood and to stimulate several types of immune cells via mucous membranes, the initial point of entry for HIV. (See paragraphs 1 and 2 of Exhibit A and paragraphs 3 and 5 of Exhibit B.)

...SeV, a key component of DNAVEC's candidate, claimed vaccine, is an RNA virus that does not cause disease in humans, is capable of efficiently delivering genes expressing HIV proteins to the immune system, and can replicate safely in the upper airway. The vaccine does not adversely affect normal cells in the body, as the vaccine components do not impact human DNA. Furthermore, the vaccine has proved highly effective in animal experiments. In particular, DNAVEC has demonstrated that monkeys that have been vaccinated intranasally using a recombinant SeV vaccine candidate can be protected against SIV, a virus that causes a disease in some non-human primates that is similar to AIDS. Finally, the vaccine is expected to provide a longer protection period than other vaccines. (See paragraph 3 of Exhibit A and paragraphs 2, 5, and 9 of Exhibit B.)

...In addition, DNAVEC has shown that the SeV vaccine not only prevents AIDS-like infections but also slows the reproduction of the virus in monkeys that are already infected. (See paragraph 6 of Exhibit B.)

...As Exhibits A, B, and C demonstrate, DNAVEC has achieved commercial success in attracting the partnership and substantial financial investment of IAVI, the world's largest institution for AIDS study and prevention, in connection with the claimed compositions and methods.

...In addition, DNAVEC has received praise by others in developing an AIDS vaccine as presently claimed. The fact that IAVI has agreed to provide billions

> of yen of financial support to DNAVEC for the development of a human vaccine for AIDS as presently claimed constitutes significant praise. Seth Berkley, CEO and president of IAVI, has stated: "Japanese biotechnology companies such as DNAVEC, with a proven capability in developing innovative vaccine concepts, will play a large role in the global search for a vaccine to end AIDS." (See paragraph 8 of Exhibit A.)
>
> ...Furthermore, DNAVEC has successfully licensed the presently-claimed SeV vaccine technology to SiBiono, a leading Chinese company. (See Exhibit C.)
>
> ...The inventive contribution of applicants in the present application has led directly to a vaccine candidate that has many of the characteristics that have long been sought in an AIDS vaccine, as described above, and that has notable advantages over other vaccines currently in clinical trials. [¶¶ 11-18 of the Hasegawa Declaration.]

In view of applicants' rebuttal evidence presented in the Hasegawa declaration and Exhibits A, B, and C, the rejections of all claims under 35 U.S.C. § 103(a) should be withdrawn.

Rejection for Obviousness-Type Double Patenting

Claims 2, 4, 16-19, 65, 66, 69, and 75 stand rejected for obviousness-type double patenting over claims 1, 4, 5, and 13 of Nagai in view of Yu, Hirsch, and Hanke.

Applicants submit that, for the reasons presented above in connection with the rejection (1), claims 2, 4, 16-19, 65, 66, 69, and 75 are non-obvious over claims 1, 4, 5, and 13 of Nagai. The obviousness-type double patenting rejection should therefore be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office Action for two months, to and including November 14, 2007.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 10/30/2007

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